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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/898,292	07/03/2001	Michele Amouyal	1231-01	2241

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IP GROUP OF DLA PIPER RUDNICK GRAY CARY US LLP
1650 MARKET ST
SUITE 4900
PHILADELPHIA, PA 19103

EXAMINER	
CALAMITA, HEATHER	
ART UNIT	**PAPER NUMBER**
1637	

DATE MAILED: 08/31/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/898,292	AMOUYAL, MICHELE	
	Examiner	Art Unit	
	Heather G. Calamita, Ph.D.	1637	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 June 2006*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *11-14,16-18,20-23 and 28* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *11-14,16-18,20-23 and 28* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments, and/or Claims

1. Amendments of June 29, 2006, have been received and entered in full. Claims 11-14, 16-18, 20-23 and 28 are pending and under examination. Any objections and rejections not reiterated below are hereby withdrawn.

Claim Interpretation

2. Claim 11 is amended to include the limitation "wherein said DNA compaction agent is present at a concentration sufficient to allow the DNA insert to remain flexible." This is read as any concentration that will permit the ligation reaction to occur.

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 11-14, 16-18, 22, 23 and 28 are rejected under 35 U.S.C. 102(b) as being anticipated by Hodgson et al. (USPN 6,410,220 B1 06/25/2002).

Hodgson et al. teach (claims 11 and 28) a method for preparing circularized recombinant nucleic acids from a vector and an insert by ligating a DNA insert and a DNA vector in the presence of a DNA compaction agent selected from the group consisting of histone proteins, histone protein derivatives, viral envelope proteins, bacterial chromoid proteins, non-histone chromosomal proteins, HMGs derivatives of

said proteins, and mixtures of said proteins and protein derivatives and selecting said circularized recombinant nucleic acid

wherein said DNA compaction agent is present at a concentration sufficient to allow the DNA insert to remain flexible and wherein said circularized recombinant nucleic acid is greater than 5kb (see col. 23 lines 17-27 and lines 22-24).

With regard to claims 12 and 27, Hodgson et al. teach the circularized recombinant nucleic acid as greater than 10 kb (see col. 23 lines 22-24).

With regard to claim 13, Hodgson et al. teach the selection steps of transferring the circularized recombinant nucleic acid into a cellular medium, cloning nucleic acid, and testing for the presence of the insert in the circularized recombinant nucleic acid (see col. 23 lines 22-27).

With regard to claim 14, Hodgson et al. teach the DNA compaction agent is selected from the group consisting of a protein, a mixture of proteins and protein derivatives exhibiting the properties of the DNA compaction agent (see col. 23 lines 49-51).

With regard to claims 16, 17, 18, Hodgson et al. teach adding a ligase to a ligation medium containing the DNA in solution in ligation buffer or adding the compaction agent to the ligation medium prior to the addition of ligase or adding the ligase and the compaction agent simultaneously (see col. 23 line 52).

With regard to claim 22, Hodgson et al. teach the ligation medium comprising a stabilizing agent that prevents denaturation, aggregation, and absorption of the DNA compaction agent (see col. 23 line 52).

With regard to claim 23, Hodgson et al. teach histone proteins (see col. 23 line 51).

Claim Rejections - 35 USC § 103

4. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

Claims 20-21 are rejected under 35 U.S.C. 103(a) as being unpatentable over Hodgson et al. (USPN 6,410,220 B1 06/25/2002) in view of Nagaki et al. (*BBRC* 246:137-141, 1998).

The teachings of Hodgson et al. are described previously.

Hodgson et al. do not teach a specific amount of HMG to use in the ligation reaction.

Nagaki et al. do teach using a range of 0.5 μg to 2.0 μg of HMG in the ligation reaction (see Fig. 2, page 139).

One of ordinary skill in the art at the time the invention was made would have been motivated to apply Nagaki's method of using a range of HMG concentrations with Hodgson's method of ligating insert and vector DNA in order to determine the amount of protein needed for the reaction. Nagaki et al. teach that HMG1 and HMG2 stimulate cohesive-end and blunt-end ligations with DNA ligase (see col. 2 2nd paragraph pp 137-138). It would have been prima facie obvious to apply Nagaki's range of HMG concentrations with Hodgson's method for ligating insert and vector DNA to achieve the expected advantage of achieving optimal ligation activity with a given amount of DNA and HMG.

Response to Arguments

5. Applicant's arguments filed June 29, 2006, have been fully considered and are not found persuasive.

Applicant argues Hodgson et al. do not anticipate the instant claims because independent claims 11 and 28 recite "wherein said DNA compaction agent is present at a concentration sufficient to allow the DNA insert to remain flexible" and Hodgson is silent with respect to the flexibility of the DNA insert in

the presence of the compaction agent. This is not persuasive because DNA condensed on a histone protein is not rigid there is no evidence the DNA insert of Hodgson does not retain flexibility. The ligation reaction of Hodgson yields a functional construct, therefore there is no evidence that the concentration of compaction agent added by Hodgson is at a concentration other than one sufficient to allow the DNA insert to remain flexible. Presumably if the concentration of compaction agent used by Hodgson resulted in rigidity of the DNA insert, the ligation reaction would be impeded because the DNA would be unable to bend and there would not be any contact between the ends of the finished vector and ligation would not occur, however again Hodgson discloses a working construct which necessitates ligation occur meaning the DNA insert was not too rigid as to impede the ligation reaction.

Applicants argue it was well known to a skilled artisan at the time of the invention that binding of histone or histone-like protein to a DNA molecule reduces DNA flexibility. Applicants support this position with the submission of two Journal articles. This argument is not persuasive because Hodgson discloses the use of dendrimers, polycations [such as polyethyleneamine] histones or liposomes not *B. pertusis* H1 homolog (addressed in the Zu publication) and Archaebacterial histone-like protein MC1 (addressed in the Cam paper). Furthermore, the submission of two papers does not sufficiently establish at the time of the invention that binding of histone or histone-like protein to a DNA molecule reduces DNA flexibility was *well known* in the art. Applicants point to both the Cam paper and the Zu paper to support the binding of histone-like protein reduces DNA flexibility. The Examiner asserts binding of any substance to a DNA molecule will necessarily reduce the molecule's flexibility to some degree and as stated above, if the concentration of compaction agent used by Hodgson resulted in rigidity of the DNA insert, the ligation reaction would be impeded because the DNA would be unable to bend and there would not be any contact between the ends of the finished vector and ligation would not occur, however Hodgson discloses a working construct which necessitates ligation occur meaning the DNA insert was not too rigid as to impede the ligation reaction, therefore the compaction agent of Hodgson is necessarily

present in a concentration sufficient to allow the DNA insert to remain flexible. Hodgson, therefore anticipates instant claims 11-14, 16-18, 22, 23 and 28 and the rejections are maintained.

With respect to the 103 (a) rejection, Applicant argues Nagaki fails to cure the deficiency of Hodgson because Nagaki do not teach or suggest a DNA compaction agent present at a concentration sufficient to allow the DNA insert to remain flexible because in Nagaki's reaction there is no DNA insert. This argument is not persuasive to overcome the 103 (a) rejections of claims 20 and 21 because Nagaki is not relied on to cure this alleged deficiency. Nagaki is relied on for the teaching of a specific amount of compaction agent to be used in a ligation reaction. As discussed above Nagaki teach using a range of 0.5 μg to 2.0 μg of HMG in the ligation reaction (see Fig. 2, page 139) which meets the concentration limitations recited in claims 20 and 21. Additionally, Nagaki et al. clearly disclose a ligation reaction in the presence of condensing reagent (see p. 139 Figure 2 and legend) and further disclose the presence of HMG 1 and HMG 2 at particular concentrations enhanced the ligation reactions (see p. 140 1st sentence under Discussion). The 103 (a) rejections are therefore maintained.

Summary

6. No claims were allowable.

Conclusion

7. **THIS ACTION IS MADE FINAL.** Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of

the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Correspondence

8. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Heather G. Calamita whose telephone number is 571.272.2876 and whose e-mail address is heather.calamita@uspto.gov. However, the office cannot guarantee security through the e-mail system nor should official papers be transmitted through this route. The examiner can normally be reached on Monday through Thursday, 7:00 AM to 5:30 PM.

If attempts to reach the examiner are unsuccessful, the examiner's supervisor, Gary Benzion can be reached at 571.272.0782.

Papers related to this application may be faxed to Group 1637 via the PTO Fax Center using the fax number 571.273.8300.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to 571.272.0547.

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hgc

TERESA E. STRZELECKA, PH.D.
PRIMARY EXAMINER

Teresa Strzelecka
8/25/06